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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/378,759 | 08/23/1999 | GARY M. FOX | 06843.0027-0 | 9481 |

7590 04/04/2002

US PATENT OPERATIONS/RBW
M/S 10-2-E-431
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| EXAMINER | |
|---|---|
| BRANNOCK, MICHAEL T | |
| **ART UNIT** | **PAPER NUMBER** |
| 1646 | 15 |

DATE MAILED: 04/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/378,759 | Fox et al. |
| **Examiner** | **Art Unit** |
| Michael Brannock, Ph.D. | 1646 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on Jan 25, 2002

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 28, 29, 31, and 36-46 is/are pending in the applica

4a) Of the above, claim(s) 28, 29, 31, 36, and 37 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 38-46 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 28, 29, 31, and 36-46 are subject to restriction and/or election requirem

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

## DETAILED ACTION

### *Status of Application: Claims and Amendments*

1. Applicant is notified that the amendments put forth in Paper 14, 1/25/02, have been entered in full.

2. Claims 28, 29, 31, 36-41 and new claims 42-46 are pending.

Claim 28 and has been amended to excluded the elected species of SEQ ID NO: 11, therefore claims 28, 29, 31, 36 and 37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

**Withdrawn Rejections:**

3. The rejection of claims 28 under 35 U.S.C. 102(b) as being anticipated by Pasquale EB, Cell Regulation 2(7)523-534, 1991, is withdrawn in view of Applicants' amendments put forth in Paper 14.

4. The rejection of claims 28, 29, 31, 35-41 under 35 U.S.C. § 101, as set forth in item 5 of Paper 12, 9/25/01, is withdrawn in view of Applicant's persuasive arguments in Paper 14 regarding the well established utility for antibodies to SEQ ID NO: 11, e.g. that they are useful for the detection of gastric cancers, as taught by the prior art reference Iwase et al., Biochem. Biophys. Res. Comm. 194(2)698-705, 1993.

**Maintained and New Rejections:**

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 38-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims require antibodies that specifically binds a polypeptide of SEQ ID NO: 11. The phrase "specifically binds" renders the bounds of the claims unascertainable because it is used in the art in a relative way to denote varying degrees of specificity. One way to obviate this rejection would be to qualify the phrase as follows:

1) An isolated antibody or fragment thereof which is raised against and specifically binds to amino acids 1 to 524 of SEQ ID NO: 11.

2) An isolated antibody or fragment thereof which is raised against and specifically binds to a polypeptide comprising SEQ ID NO: 11.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 43 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims require a pharmaceutical composition comprising a therapeutically effective amount of an antibody, yet the specification does provide sufficient guidance as to what the antibody is therapeutically effective for; and neither can such a use be reasonably inferred from the prior art. While the instant antibodies have a utility and an enabled use to detect elevated levels of Hek5 as diagnostic of gastric cancer (see Iwase et al., Biochem. Biophys. Res. Comm. 194(2)698-705, 1993, discussed below), there does not appear to be evidence of a correlation between interfering with Hek5 by binding and corresponding abrogation of cancer. There is no evidence that Hek5 is causative of cancer, only correlative with it's presence, i.e. it could be that the upregulation of Hek5 observed by Iwase et al. is a result of changes associated with transformation and not a participating cause itself. Thus, the specification has not taught how to use an antibody that is therapeutically effective for the treatment of any condition; and nor has the specification taught how to make such an antibody.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 38 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Pasquale EB, Cell Regulation 2(7)523-534, 1991, see Information Disclosure Statement of Paper number 2.

Pasquale disclose polyclonal antibodies that specifically bind Cek5 (see the Abstract). The Cek5 polypeptide is 95% identical to the instant SEQ ID NO: 11, see the attached sequence alignment. Therefore, absent evidence to the contrary, the polyclonal antibodies disclosed by Pasquale are expected to specifically bind to the polypeptide of SEQ ID NO: 11.

Applicant argues that a polyclonal serum raised against a B-gal fusion of amino acids 167-926 of Cek5 is not the same as an antibody that specially binds to "a polypeptide comprising amino acids 1-524 of SEQ ID NO: 11", because a large portion of the antibodies in the polyclonal serum raised to the Cek5 fusion would recognize the transmembrane and intracellular domains and therefore would not "specifically bind" the extracellular domain. This argument has been fully considered but not deemed persuasive for two reasons. First, the phrase "specifically binds to", is used in the art in a relative way to denote varying degrees of specificity, e.g it can be used to indicate that an antibody recognizes primarily a single amino acid sequence

or closely related sequences. The phrase, alone, however does not exclude binding to other sequences, and there does not appear to be any other definition of the phrase in the specification. Second, the claims do not require that the antibodies specifically bind the sequences contained only within residues 1-524 of SEQ ID NO: 11 as Applicant appears to suggest. The claims require only that the antibodies be capable of specifically binding to a "polypeptide *comprising* amino acids 1-524 of SEQ ID NO: 11". It is suggested to Applicant that the specification, in Example 4, teaches *raising* antibodies to the extracellular domain of Hek5. The claim can be modified so that it does not read on Pasquale's antibodies by specifying what the instant antibodies are raised to. Below are two samples claims that overcome that problem.

1) An isolated antibody or fragment thereof which is raised against and specifically binds to amino acids 1 to 524 of SEQ ID NO: 11.

2) An isolated antibody or fragment thereof which is raised against and specifically binds to a polypeptide comprising SEQ ID NO: 11.

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 40-42, 44, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pasquale EB, Cell Regulation 2(7)523-534, 1991, as applied to claims 38 and 39 above, in view of U.S. Patent No: 4816567.

Claims 40-42, 44, and 45 require the antibody of claims 38 and 39 yet claims 40-46 also require that the antibody be a monoclonal, chimeric, or CDR grafted antibody. 4816567 teaches that in the art of antibody production, monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies are more preferred, see col 2, lines 40-65 and cols 15 D.6 and D.7).

Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made, with reasonable expectation of success, to make a monoclonal, chimeric, or CDR grafted antibodies according to U.S. Patent No: 4816567 when practicing the invention of Pasquale EB. The motivation to do so is provided by U.S. Patent No: 4816567 wherein in is indicated that in the art of antibody production, monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies are more preferred, see col 2, lines 40-65 and cols 15 D.6 and D.7).

13. Claims 38-42, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iwase et al., Biochem. Biophys. Res. Comm. 194(2)698-705, 1993 in view of U.S. Patent No: 4816567.

Applicant asserts (Paper 14) that the polypeptide taught by Iwase et al., is the polypeptide of the instant SEQ ID NO: 11. Iwase et al., teach that the polypeptide (H1) is dramatically up regulated in human gastric cancers and the dysregulation of the expression of the polypeptide is probably involved in the development of these gastric cancers. Iwase et al. do not specifically discuss antibodies to the polypeptide, however it is well appreciated by one of ordinary skill in the art that such antibodies would be useful for diagnosis of gastric cancers as taught by Iwase et al. U.S. Patent No: 4816567 teaches that in the art of antibody production, monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies are more preferred, see col 2, lines 40-65 and cols 15 D.6 and D.7).

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to make monoclonal antibodies, CDR grafted and otherwise chimeric antibodies to the polypeptide taught by Iwase et al. The desire for diagnosis of gastric cancers, being self evident from the teachings of Iwase et al., while the motivation to make monoclonal, CDR grafted, or otherwise chimeric antibodies is provided by U.S. Patent No: 4816567 wherein it is indicated that in the art of antibody production, monoclonal antibodies are generally

preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies are more preferred, see col 2, lines 40-65 and cols 15 D.6 and D.7).

***Conclusion***

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

April 3, 2002

YVONNE EYLER, PH.D
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